Endocrine

434 Physiology team
presents to you:

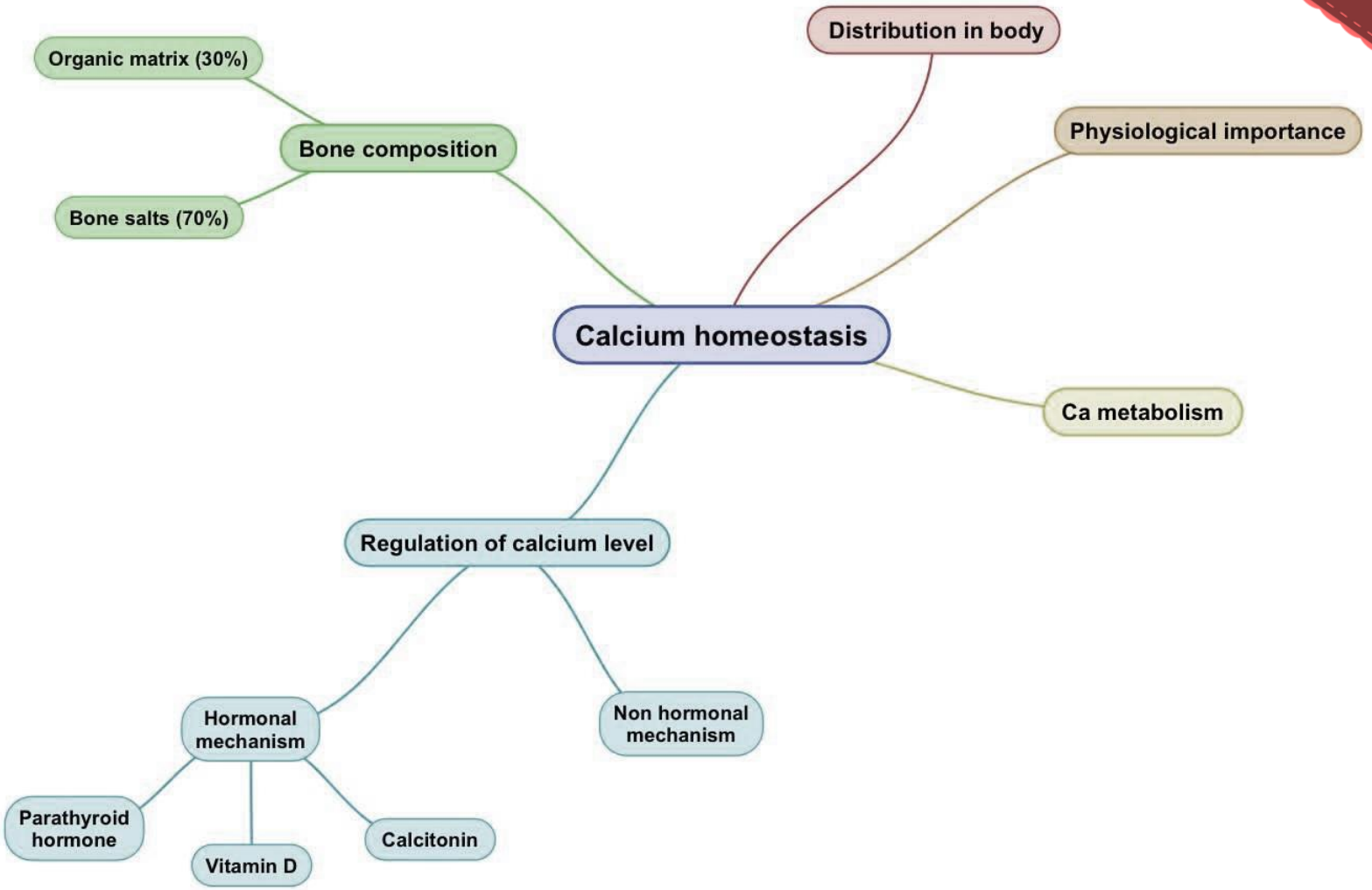
Calcium Homeostasis

- Important
- Further explanation

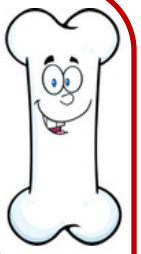
Contents

Please check out this link before viewing the file to know if there are any additions/changes or corrections. The same link will be used for all of our work [Physiology Edit]

Mindmap


Calcium homeostasis
Distribution in body
Physiological importance
Ca metabolism
Bone composition
Organic matrix (30%)
Bone salts (70%)
Regulation of calcium level
Hormonal mechanism
Non hormonal mechanism
Parathyroid hormone
Vitamin D
Calcitonin

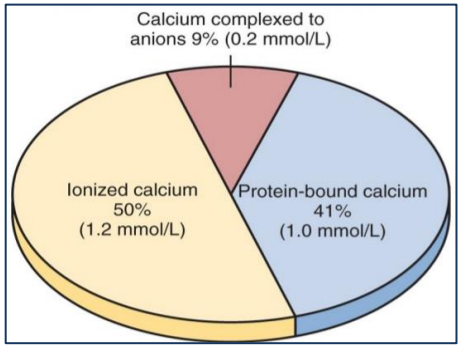
Distribution of Ca++ in Body



- 0.1 % ECF
- 1 % ICF (Endoplasmic Reticulum)
- 99 % Bone & teeth

TABLE 36.1 Body Content and Tissue Distribution of Calcium and Phosphorus in a Healthy Adult

	Calcium	Phosphorus
Total Body Content	1,300 g	600 g
Relative Tissue Distribution (% of total body content)		
Bones and teeth	99%	86%
Extracellular fluid	0.1%	0.08%
Intracellular fluid	1.0%	14%



Distribution of Ca++ in ECF

Total plasma calcium = 9-10.5 mg/d

59%

41%

Diffusible calcium

Non- diffusible calcium

50%

9 %

Ionized

complexed

Protein bound

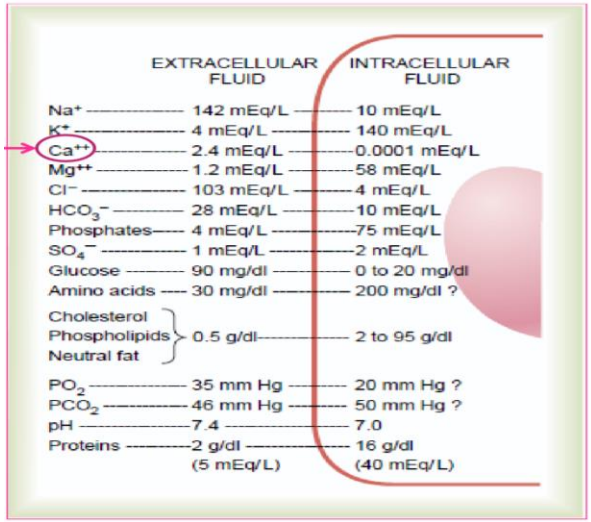
Protein-bound calcium

Most of this calcium is bound to albumin & much smaller fraction is bound to globulin

- Binding of calcium to albumin is pH-dependent
- Acute respiratory alkalosis increases calcium binding to protein thereby decreases ionized calcium level

Physiological importance of Calcium :

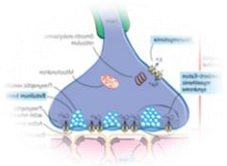
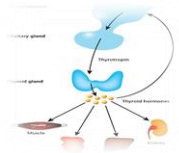
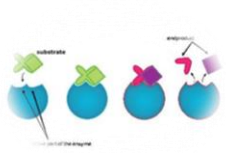
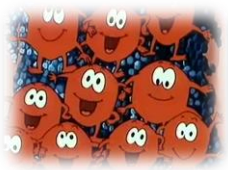
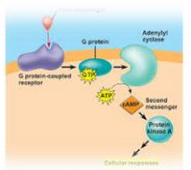
Calcium salts in bone provide structural integrity of the skeleton



Why is the ECF calcium more than the ICF Ca although we mentioned that ECF is 0.1% and ICF is 1%?
Because Ca is in the endoplasmic reticulum not free in the cellular cytoplasm

Calcium ions in extracellular and cellular fluids is essential to normal function for the biochemical processes

- Neuromuscular excitability
- Hormonal secretion
- Enzymatic regulation
- Blood coagulation
- Second messenger

Phosphate

Phosphorous is an essential mineral necessary for ATP and cAMP second messenger systems

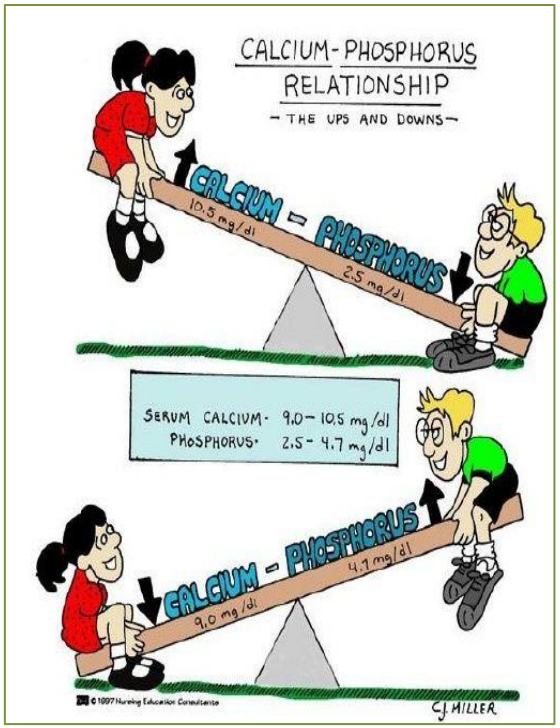
plasma concentration is around 4 mg/dL.

Calcium is tightly regulated with Phosphorous in the body

Daily requirements of calcium

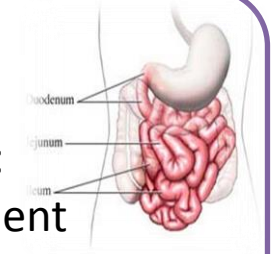
Infants & adults: 12.5 -25 mmol/day

•Pregnancy, •lactation •after menopause: 25-35 mmol/day



Absorption of calcium

- Duodenum: active transport
- small intestine: concentration gradient

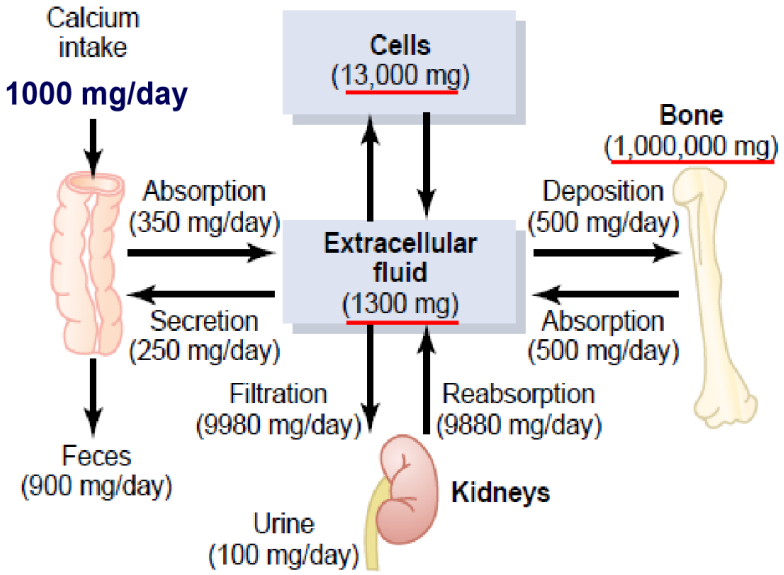


Calcium is poorly absorbed from G.I

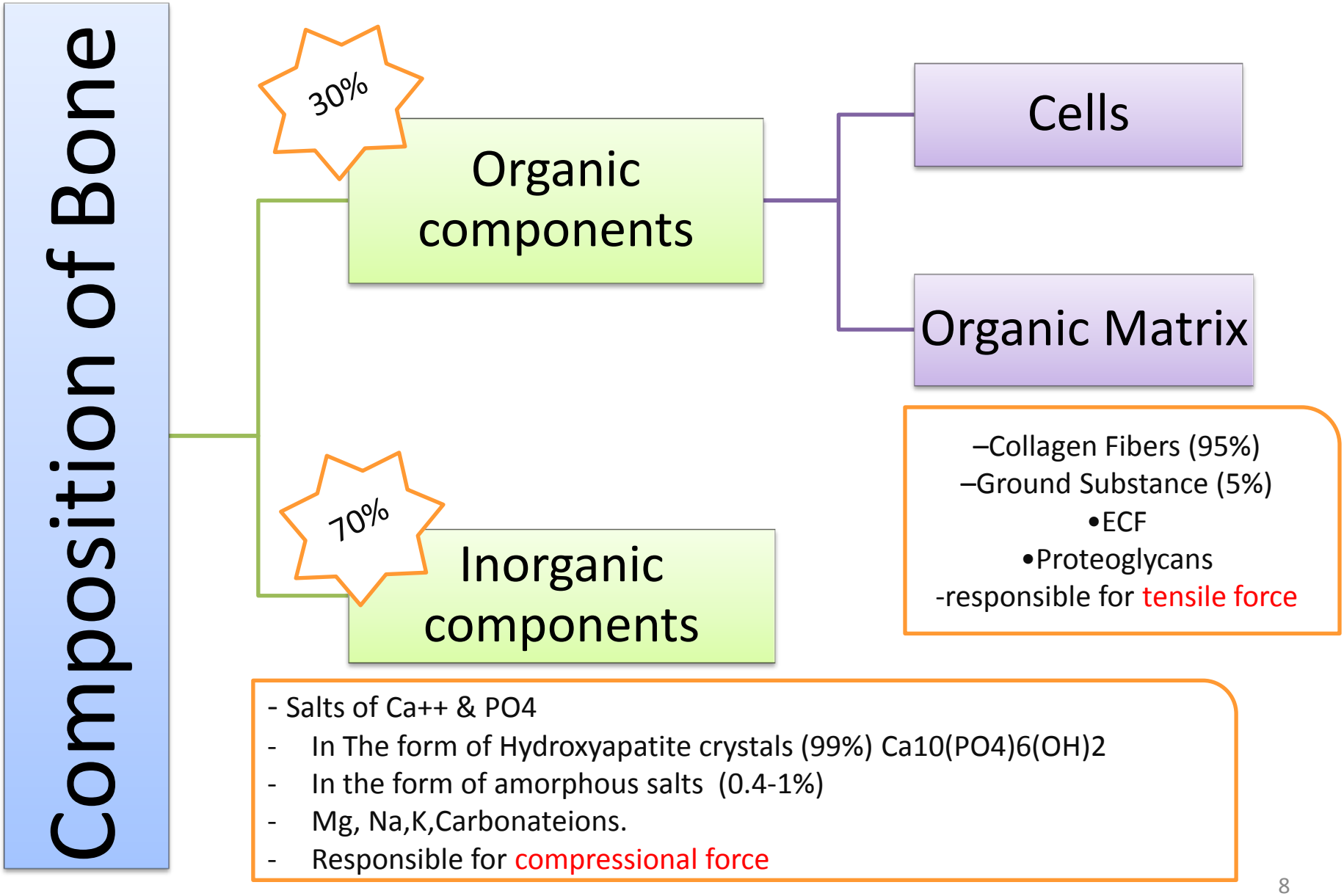
Calcium metabolism

Further explanation :
If the person ingests 1000 mg of elemental calcium daily, approximately 350 mg is absorbed from the GIT, a process that is stimulated by active form of vitamin D 1,25-dihydroxycholecalciferol . However , about 250 mg is secreted into GIT . Thus net absorption of calcium is 100 mg / day (350 mg -250 mg) , and the remaining 900 mg day (of the 1000 mg ingested) is excreted in feces . The absorbed Ca enters the Ca in ECF .

Calcium Metabolism in an adult human



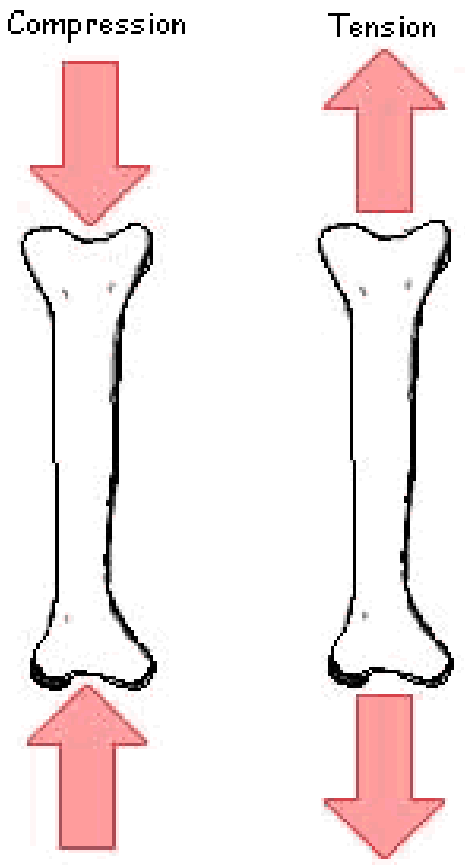
Physiology of Bone



Physiology of Bone

Several properties contribute to the strength of bone :

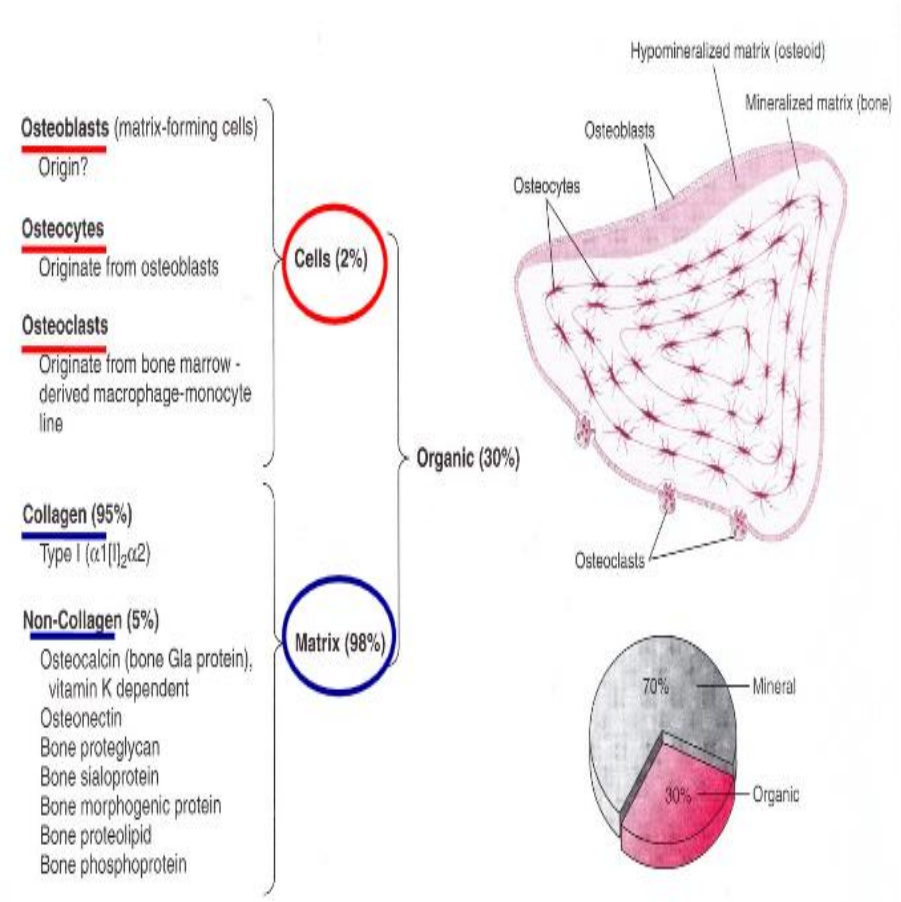
- Collagen contributes to the tensile force of bone.
  measured by the maximum stress that a material can withstand while being stretched or pulled.
- Bone salts contributes to the compressional forces of bone .



Doctor Abeer's explanation:
if we remove the calcium from the bone (no compressional force) → يصير العظم لين وينحني
And if we heat the bone and remove the organic matrix → no tensile force → the bone becomes brittle (هش)

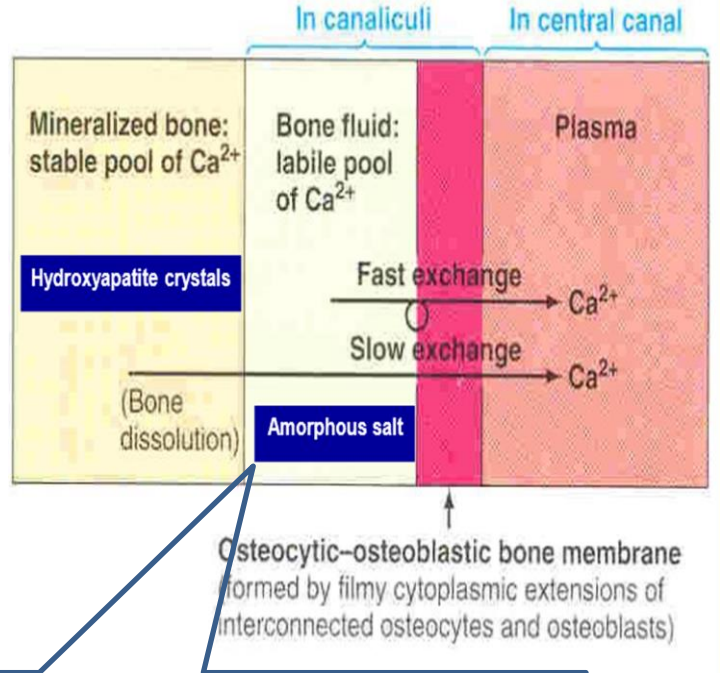
Physiology of Bone

Organic Components



Inorganic components

Don't skip this picture!



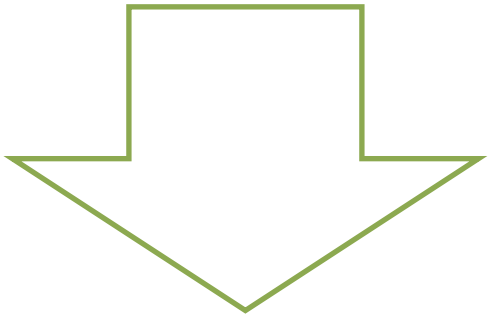
A type of exchangeable calcium, represents (0.4-1%) of bone salts. Always in equilibrium with Ca^{2}+ in ECF so involved in the rapid regulation ionized Ca++ level in ECF.

- Amorphous salt is found in **bone fluid** & hyrdoxyapatite crystals are in the **minralized bone**
- Calcium is restored to circulation by amorphous salt in **short term regulation**
- Mineralized bone (hydroxyapatite crystals) are used in **long term regulation**

Regulation of calcium

Normal plasma level of Calcium is : 9-10.5 mg/dl

Any disturbance of this range could cause diseases



Renal stones

(Deposition)

Hypercalcaemia leads to Renal stones

Hypocalcaemia leads to tetany

Tetany

(Excited nervous system)

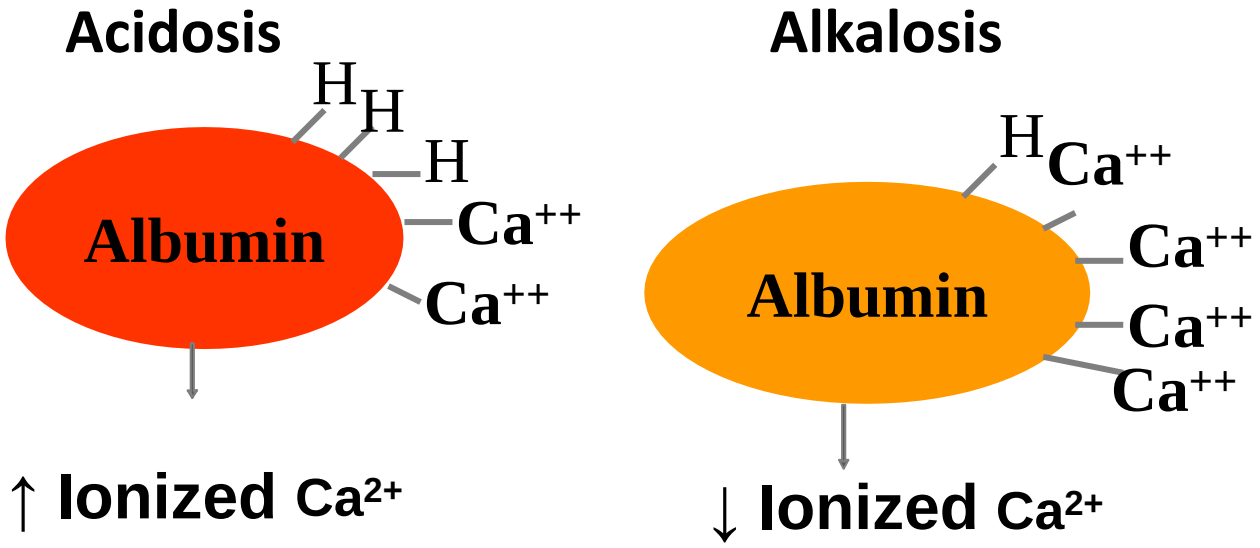
Keep in mind that:

↓ Ca+2 in ECF → excited nervous system (muscles contraction)

↑ Ca+2 in ECF → depressed nervous system (muscles relaxed)

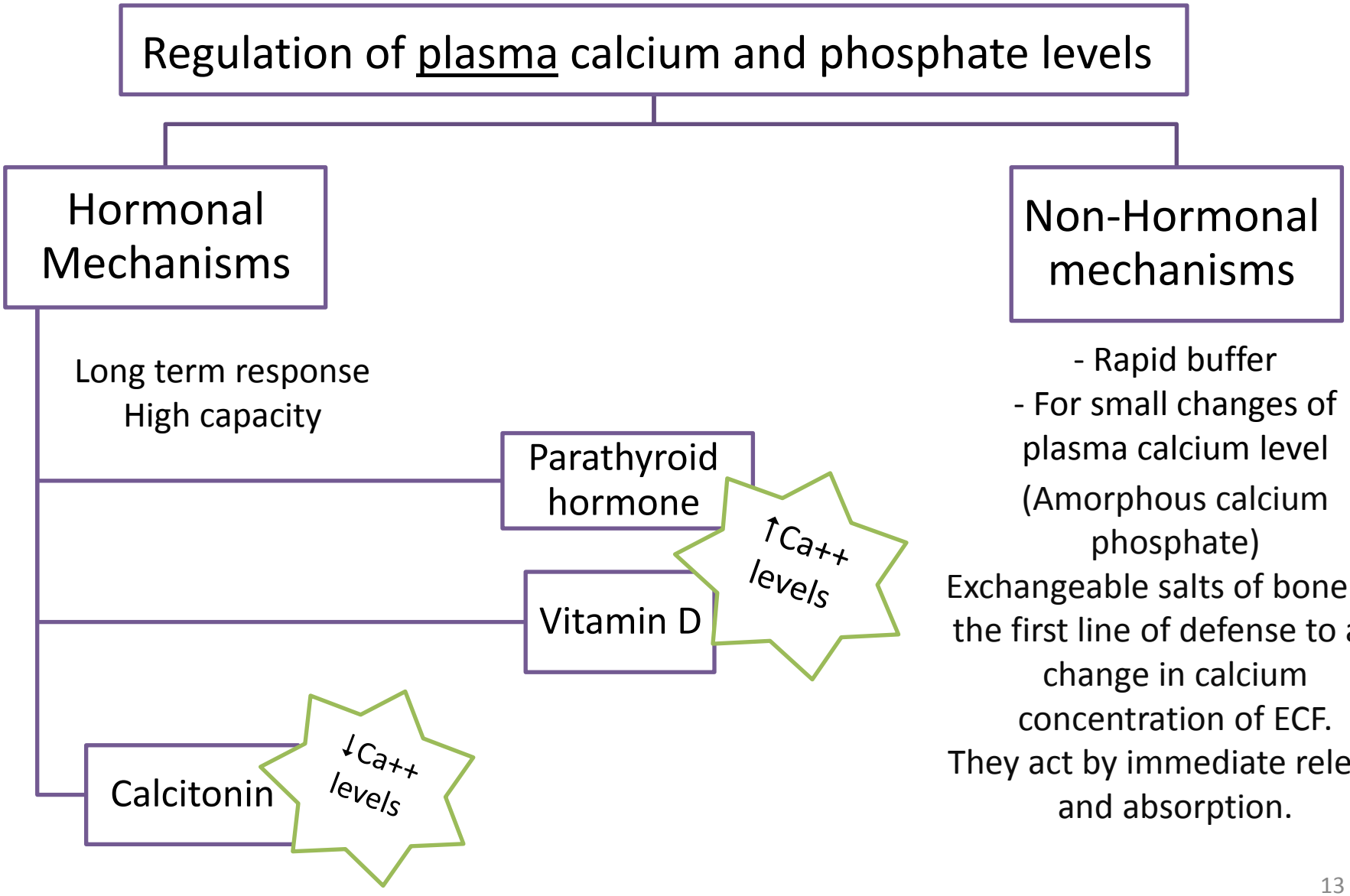
Regulation of calcium

- Increase in protein concentration → ↑ in total Ca2+ concentration
- Decrease in protein concentration → ↓ in total Ca2+ concentration
- The effects on ionized Ca+2 concentration are insignificant
- Changes in anion concentration alter the ionized Ca2+ concentration e.g. ↑ plasma phosphate con. → ↑ in the conc. of Ca2+ complexed to phosphate → ↓ ionized Ca2+ concentration
- Ca2+ affects Na permeability of nerve membranes.
- ↓ plasma Ca2+ → generation of spontaneous action potentials in nerves → tetany
- Acid-base abnormalities alter the ionized Ca2+ conc. by changing the fraction of Ca2+ bound to plasma albumin
- Albumin has negatively charged sites, which can bind either H+ ions or Ca2+ ions



Hyperventilation → Respiratory alkalosis → ↓ ionized Ca2+ → Tetany

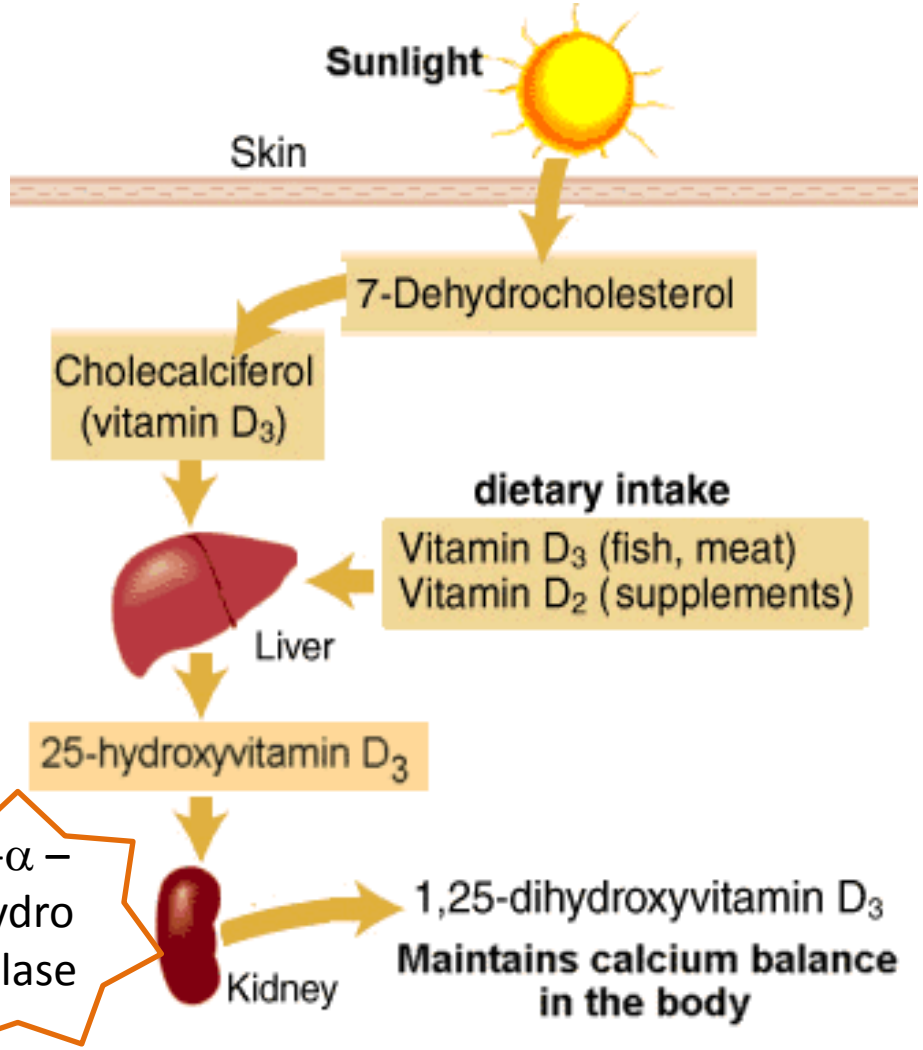
Regulation of calcium



Regulation of calcium

Hormonal Mechanisms : Vitamin D (1,25 Dihydroxycholecalciferol)

The biologically active form of vitamin D is 1,25-dihydroxycholecalciferol (calcitriol) , and it is synthesized by the hydroxylation of 25-hydroxycholecalciferol by the enzyme 1-α –hydroxylase in the kidney.
Vitamin D synthesis is discussed in details in biochemistry lecture



- **Low plasma Calcium levels**
- **Parathyroid Hormone**
- **Prolactin**

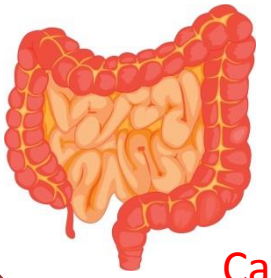
Regulation of calcium

Hormonal Mechanisms : Vitamin D (1,25 Dihydroxycholecalciferol)

1- Bones

-In small quantities promotes bone mineralization

-In large quantities promotes bone resorption by : 1-↑PTH action 2-↑Number & activity of osteoclast



2- Epithelial cells of small intestine

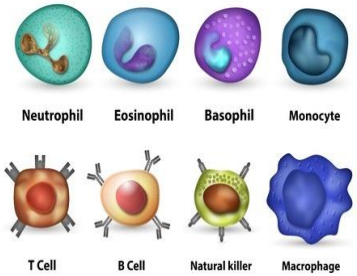
Has a potent effect to increase calcium & phosphate absorption by :

1- Induces the synthesis of Calcium binding protein(calbindin).

2- formation of Calcium-stimulated ATPase.

3-Alkaline phosphatase.

Functions of Vit D

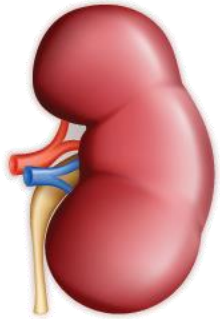


4- Immune system

Stimulate differentiation of immune cells

3- Kidneys

Increases Renal calcium and Phosphate absorption

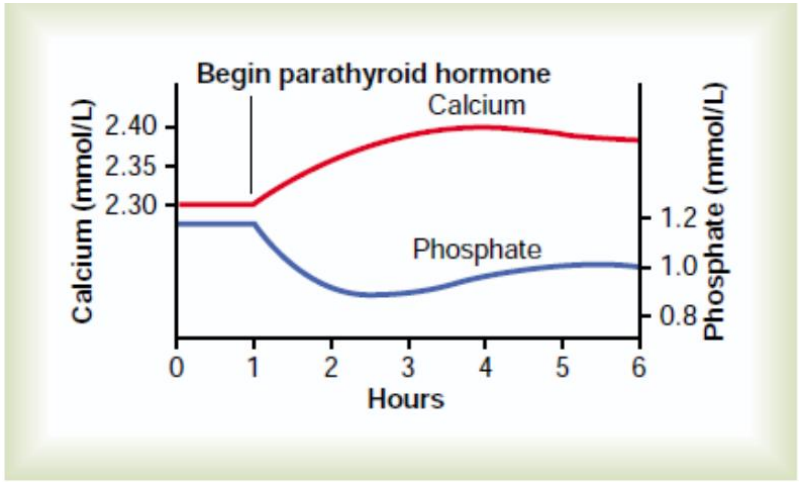


Regulation of calcium

Parathyroid hormone

- **Source:** Parathyroid gland
- **Stimulated by** hypocalcaemia
- **Polypeptide hormone:** (84 aa)
- **Molecular Weight:** 9500
- **Half Life:** 10 min
- **Mechanism of action:** acts via 2nd messenger mechanism utilizing cAMP
- **Acts on:** Bone, kidney, and intestine
- **Action:** Necessary for fine control of ionized serum levels. Increases plasma Ca++ levels & decreases phosphate levels

PTH ID

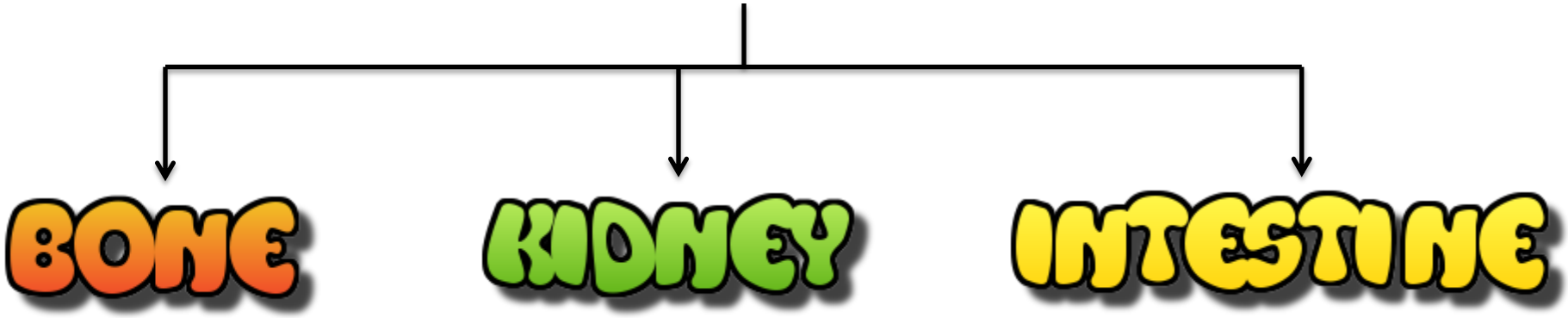


Extra explanation for PTH effects (guyton):
It has 2 principle effects:

1) ↑ calcium & phosphate absorption from the bone
2) ↓ calcium excretion & ↑ phosphate excretion by the kidneys

The net result on phosphate is decrease because the effect of PTH in increasing renal phosphate excretion is greater than phosphate absorption from the bones i.e. 2nd point is stronger than the 1st point.

Parathyroid Hormone Effects



- Parathyroid hormone acts **directly** on bones to stimulate resorption and release of Ca^{2+} into the extracellular space (slow)
- Acts **directly** on the kidney by:
  1. ↓ phosphate reabsorption from the proximal convoluted tubules (phosphaturic action). Phosphate excretion in the urine plasma phosphate concentration (rapid)
  2. ↑ Ca++ & Mg ions reabsorption from the distal convoluted tubules, collection ducts and ascending loop of Henle.
  3. ↑ Formation of 1,25 vit D3 in the kidney.
- ↑ absorption of calcium and phosphate **indirectly** through stimulating formation of 1,25 – (OH)2 -D3 in kidney

Pay attention:
If they ask about PTH stimulus: the answer is calcium DECREASE
If they ask about PTH effect: the answer will be calcium INCREASE

Regulation of calcium

Calcitonin

- **Source:** Secreted by the parafollicular cells (C cells) of the thyroid gland.
- **Stimulated by** hypercalcaemia
- **Nature:** 32 amino acid peptide.
- **Functions:**
  - Decrease blood Ca++ level very rapidly within minutes.
  - Opposite effect to PTH Stimulus for secretion: Increased plasma calcium concentration

Calcitonin action

On Bones

[1]↑Ca++ deposition of bone
[2] Inhibits Bone resorption by:
- inhibition of osteoclasts
- ↓ formation of osteoclasts

On Kidneys

↓ Ca++ reabsorption
↑ Ca++ excretion (in addition to phosphate)

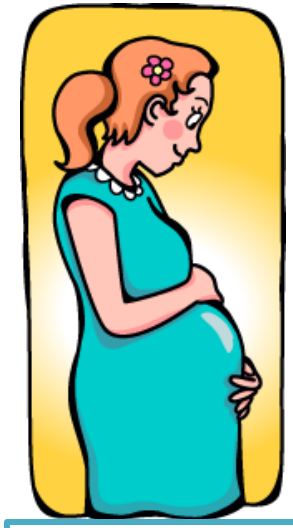
Other causes of ↑ calcitonin secretion:
1- Estrogen
2- gastrin
3- glucagon
4- secretin
5- CCK
6- beta-adrenergic stimulation

Regulation of calcium

Other regulators

Estrogen

- Stimulates osteoblast activity
- limits osteoclast activity
- enhance PTH secretion
- Estrogens changes the set point of PTH cells in the parathyroid so a greater reduction of Ca2+ is needed to increase PTH secretion so: Estrogen decreases Ca2+ loss from bones

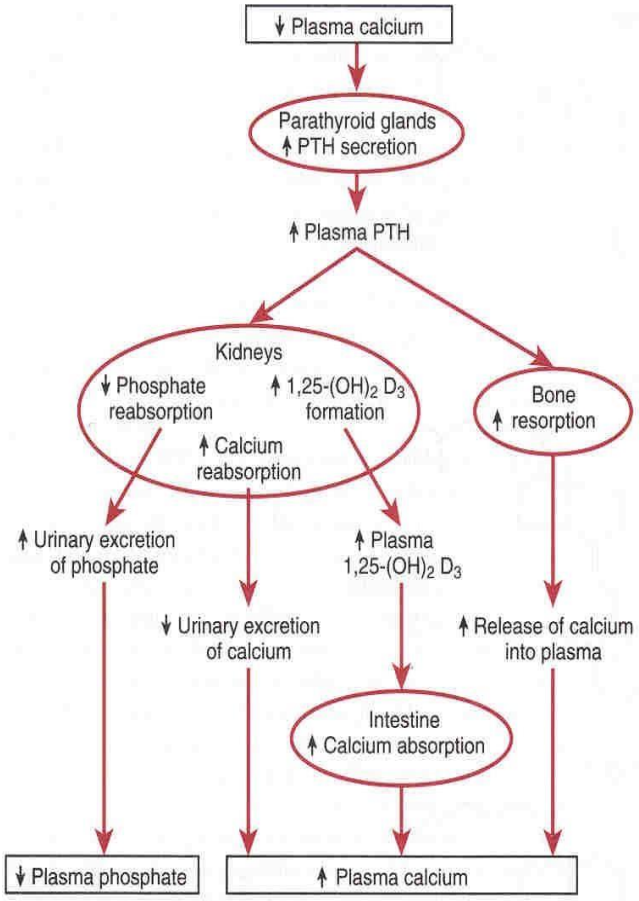


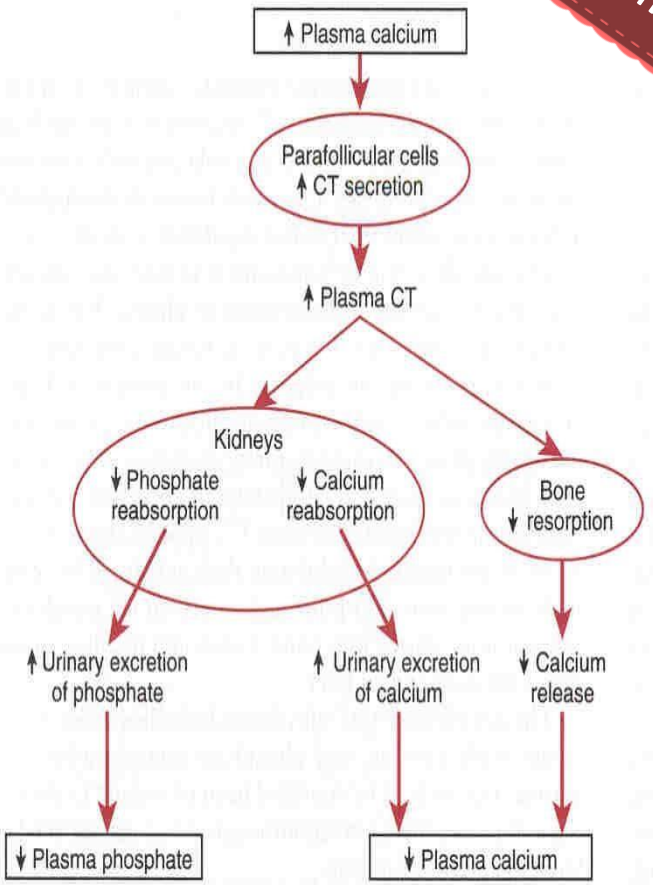
Pregnancy & lactation

- The daily required dose of Ca2+ is greatly increased during pregnancy.
- 30 grams of Ca2+ are transferred to the fetus and lost in urine during pregnancy
- Bone turn over is increased during pregnancy → osteoporosis especially hip bone.
- 280 – 800 mg of Ca2+ are lost in breast milk per day during lactation
- The mother compensates by:
  - ↑ intestinal absorption
  - ↓ renal excretion
  - ↑ bone resorption

General comparison between PTH & Calcitonin

Summary





Hormone	Parathyroid hormone	Calcitonin
Source	Parathyroid gland	Thyroid gland (c-cells)
Stimulus	hypocalcaemia	hypercalcaemia
Effect	Increase plasma calcium	Decrease plasma calcium

Answer key: 1-C 2-A 3-C 4-B 5-D 6-A 7-B

MCQs

1-Which of the following is not involved in the regulation of Vitamin D?

A. PTH
B. Prolactin
C. Alkaline phosphate
D. Serum phosphate

2- What type of collagen represents the majority of bone matrix ?

A. Type 1
B. Type 2
C. Type 3
D. Type 4

3- which of the following is an effect of vitamin D ?

A. High blood calcium levels and low Phosphate
B. Low phosphate and calcium blood levels
C. High calcium and phosphate blood level
D. Low calcium and High phosphate blood level

4- Which one of the following is a normal level of plasma calcium ?

A. 6 mg/dl
B. 10 mg/dl
C. 8 mg/dl
D. 12mg/dl

5-Which of the following hormones is not important in calcium homeostasis ?

A. Calcitonin
B. Parathyroid hormone
C. 1,25-dihydrocycholecalciferol
D. Glucagon

6- which one of the following structures has the maximum percentage of total body Ca ?

A. bones
B. Skeletal muscle
C. plasma
D. blood

7-which one of the following hormones is essential for the absorption of Ca from small intestine ?

A. Thyroxine
B. 1,25-dihydrocycholecalciferol
C. calcitonin

SAQs

Q1: What is the function of Vitamin D ?

Ans: To Increase blood calcium level .

Q2: How vitamin D is involved in the resorption of bone ?

Ans: 1- by facilitating the PTH action on bone 2- by increasing the action and numbers of osteoclast

Q3: By which mechanism does PTH increase stimulate Vitamin D action ?

Ans: By stimulation the hormone 1-α –hydroxylase in the kidney .

Q4: How amorphous salts involved in regulating calcium level ?

Ans: Depending on the level of calcium in the ECF , they exchange to be in equilibrium .
So when ECF calcium level goes down they are released from bone , and when it goes up they will be absorbed again to the bone.

Q5: what are the functions of calcium in our body ?

Ans: Neuromuscular excitability – Hormonal secretion – Enzymatic regulation – Blood coagulation – Second messenger

Q6: what happens to calcium in case of acute respiratory alkalosis ?

Ans: increases calcium binding to protein & decreases ionized calcium level .

Thanks for checking our work

Good Luck

Done by:

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Luluh Aldaej
Lina Aljurf